

# Liposomal Cosmeceuticals as Skin Protectives and Curatives

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## ABSTRACT

Lifestyles and environmental changes draw people away from healthy and natural-looking skin. To hide the impaired and damaged skin texture as a result of several factors, people mostly prefer decorative cosmetics to get an immediate but temporary result. To overcome this problem, cosmeceuticals are emerged containing skin-protective and curative agents in a cosmetic base. The market is full of skincare products and many of them have proven unsatisfactory to the consumer. Liposome, a novel lipoidal carrier, overcome the limitations of conventional therapies. Liposomes are proven to deliver a wide variety of drug cargo to the targeted skin layer with negligible drug loss. This delivery platform got wide acceptability among users due to its remarkable efficacy and safety. Many more evolutions occurred in conventional liposomes over time and it is still an area of interest for researchers. To date, it has given outstanding performance in the broad areas of skincare and has grabbed the global skincare market in a short span of time. As this approach is evolving rapidly, developed countries have set their own separate protocols regarding nano-materials used in cosmetics. The present review focuses on newer liposomal cosmeceuticals and their actives as skin protectives and curatives.

**Keywords:** Cosmeceutical, Skin care, Skin protective, Curative, Liposomes.

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## INTRODUCTION

Skin is a primary shielding organ of our body that protects us from outside stimuli. It boosts self-confidence in a man or woman by adding a valuable contribution to the persona of a human being.<sup>1</sup> As it is the primary organ that is exposed to the external environment, it is more prone to several skin complications. Causative factors like lifestyle changes, food habits, external stressors and internal stressors affect the natural integrity of the skin and aggravate skin complications such as uneven skin, oily skin, dry skin, hyperpigmentation, slack skin, ageing, cellulite, further, sensitive skin is associated with sunburn and acne. Initially, there had been only a few evolutions in the skin care industry. In the early 1970, the borderline among cosmetics and dermatological merchandise started vanishing and cosmetics transformed into medicines. Industries started producing healing merchandise called over the counter drugs or cosmeceuticals.<sup>2,3</sup> Skin care is not only confined to the productive population but also the geriatric populace, who require additional skin care as they are afflicted by skin illnesses due to altered physiology of the skin.<sup>4</sup> The currently available invasive as well as non-invasive skin care therapies, have pros and cons. Invasive therapies

impact the cell, extracellular matrix and modify the function and architecture of treated tissue. Non-invasive chemical treatments like conventional cream, gels, lotion, ointment, drug solution are associated with limitations such as inter-intrasubject variability, due to the enzyme present in the skin, skin irritation and skin sensitization.<sup>5,6</sup>

Liposomes as vesicular systems are considered to be suitable for drug delivery via the skin as they can overcome drawbacks like local irritation, itching, erythema, low permeability of medicine in the horny layer. Another rising area that contributes to skin fitness is nutricosmetics, a combination of health and beauty products that mainly contain herbs and liposomal carrier to maintain natural integrity and garnish skin. Skin care cosmetics are distinguished as protective and curative.<sup>7</sup> The present review article reviews skin-protective and curative liposomes along with active molecules contributing to skin health, market for skin care liposomes, and regulatory aspects.

## LIPOSOMES AS A CARRIER VESICLE

British haematologist Alec D. Bangham introduced liposome as an artificial, amphiphilic, and microscopic carrier with a unique framework. The first liposomal product in the cosmetic industry was Capture TM, an anti-ageing gel for the face by Christian Dior in 1987. Nano-to micron-sized spherical liposomes serve as an inert carrier capable of housing hydrophilic as well as hydrophobic entities. It is biocompatible and it anchors and fuses with the cell



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membrane to deliver the content of the vesicular system for a prolonged period of time.<sup>8,9</sup> The delivery of liposomes through skin relies on the ability of liposomes to permeate to the depth of the skin. Figure 1 represents the mechanisms of transportation of liposomes through the skin.

## LIPOSOMES IN SKINCARE COSMECEUTICALS

Traditional liposomes are known to remain intact in the epidermis of the skin with disrupted stratum corneum in eczema but cannot penetrate the skin with hyperkeratosis in psoriasis. Traditional liposome does not penetrate beyond the stratum corneum of healthy skin.<sup>10</sup> Alteration in the morphology of the conventional liposomes results in modern vesicles that are depicted in Figure 2, which are proved to be more fruitful than the conventional one. Ethosomes are liposomes containing ethanol at a 20-45% concentration that gain entry into the skin by reversibly disturbing the intercellular lipid and transferring the active molecules to the site of action. Liposomes transformed into transferosomes by incorporation of edge activators into the lipid bilayer membrane aid in passage through the skin barrier. They are metastable and have an ultra-flexible membrane. It makes the system reach the deeper skin layers. The high hydrophilicity and flexibility of the transferosome prevent aggregation of vesicles. Transethosome consists of 30% ethanol and an edge activator. It is a hybrid of the transferosome and the ethosome. Hence, its mechanism of action is a fusion of both systems.<sup>11,12</sup>

Leciplex and catezome possess a cationic surface charge. Catezome is a carrier that conveys active ingredients superficially, as in the case of sunscreen, fragrances and proteins, which could lead to irritation and impaired sensation if they approach the lower layer of skin. They have better stability at room temperature for 18 months.<sup>13</sup> In contrast to this, leciplex could access the deeper layer of the skin due to electrostatic attraction to the negatively charged skin surface.<sup>14</sup>

Niosomes are comprised of non-ionic surfactants and are preferred vesicles in skin care formulations because of their non-toxic nature and great stability.<sup>9</sup>

Pharmacosomes are neutral molecules possessing both cationic and anionic charges, water-loving and lipid-loving properties. They contain an agreeable ratio of polyphenol to phospholipids. Poorly soluble drugs are dispersed in the pharmacosome system by sharing electron pairs, electrostatic forces of attraction, or by forming hydrogen bonds with lipids.<sup>15</sup>

Cyclodextrin-based liposomes possess a hydrophobic cavity and a hydrophilic surface that form inclusion complexes with many poorly soluble hydrophobic drugs, thus enhancing their skin targeting and bioavailability. Liposomes protect the cyclodextrin-drug inclusion complex until the drug is released, thus decreasing skin irritation.<sup>16</sup>

Nanotopes are smaller particles that exist in the range of 20-40 nanometers. It possesses better stability over liposomes. It is composed of a suitable ratio of conventional phospholipids such as lecithin and co-surfactants. It enables the formation of an uninterrupted layer from the lipidic centre to the exterior aqueous phase by the interposition of co-surfactants into the lecithin molecules. In contrast to liposomes, nanotopes contain a dominant ratio of membrane phospholipids to the entrapped drug. This system is mainly used to accommodate cosmetically active agents such as Vitamin-A, tocopherol and requires less distortion energy during penetration into the skin.<sup>17</sup>

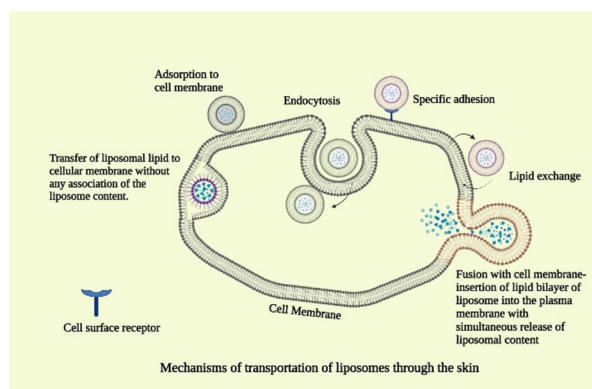
## APPLICATIONS OF LIPOSOMES IN SKIN CARE

The application of liposomes in skin care is a vast area. The focus of the present article is on the curative skin care products which include antiacne, skin whitening and protective categories which include skin moisturiser and sunscreen. Figure 3 summarises role of liposomes along with mechanism of action in protective and curative therapy.

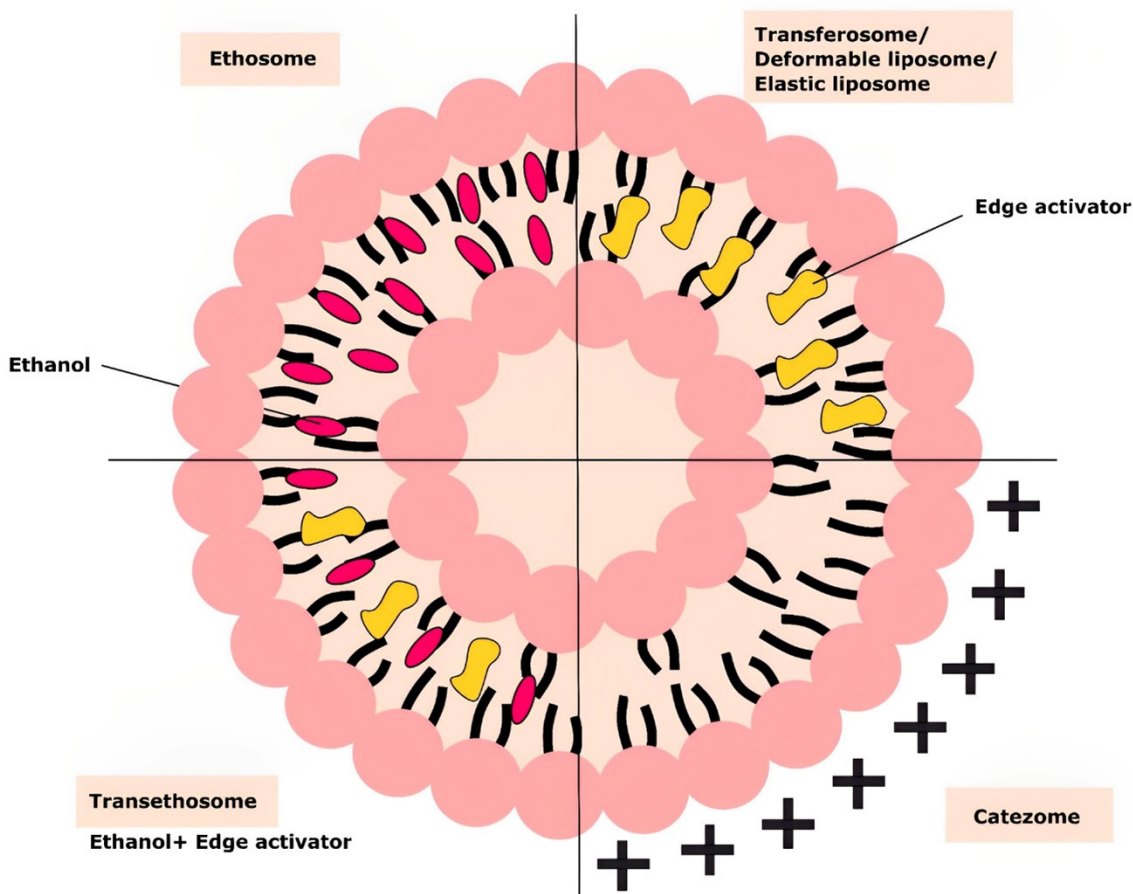
### Liposomes in Acne Therapy

Acne affects 85% of the global populace and is most widespread in teenagers and younger. The causative elements of acne are an overactive pilosebaceous unit, hyperkeratinisation of the horny layer of the skin, colonisation and multiplication of *Propionibacterium acnes* (*P.acnes*) in an anaerobic atmosphere built by the clogged pores.<sup>18</sup>

The acne therapies include use of sebum suppressive agents, keratolytic, antibacterial and hormonal treatments. The prolonged use of antibiotics such as broad-spectrum tetracycline, minocycline and narrow-spectrum erythromycin develops resistance against acne causing pathogens. The concurrent use of broad-spectrum antibacterial agents that are equally active against sensitive and resistant strains of pathogens is essential to safeguard the efficacy of antibiotics.<sup>19</sup> In the antibacterial evaluation of Dipalmitoylphosphatidylcholine (DPPC) based liposomes encapsulated with tetracycline and tretinoin



**Figure 1:** Mechanisms of transportation of liposomes through the skin.



**Figure 2:** Modified forms of liposomes.

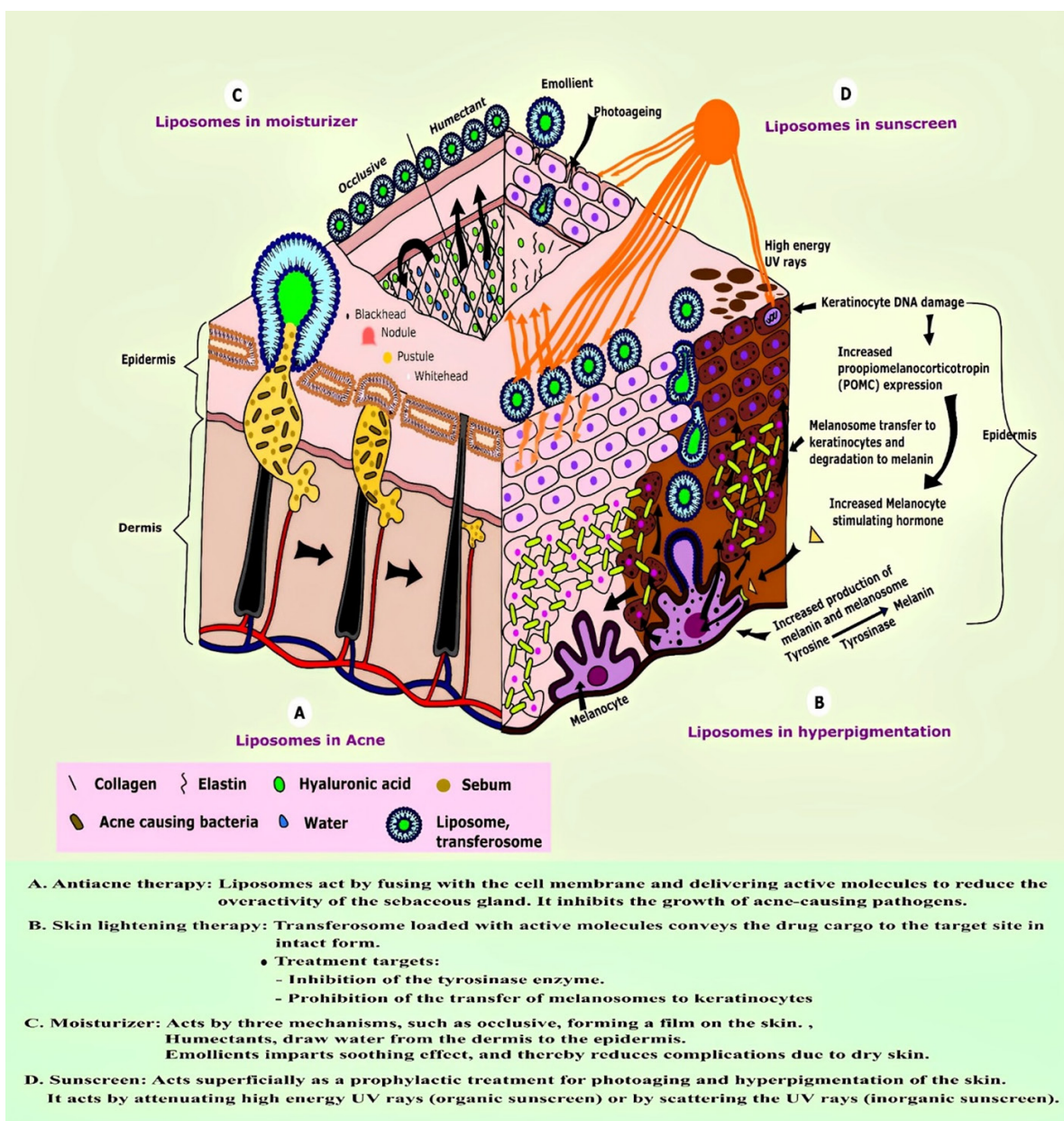
against *Staphylococcus aureus* ATCC29213 and *Staphylococcus epidermidis* ATCC 35984 strains, the Minimum Inhibitory Concentration (MIC) value was observed to be 0.016 mcg/ml for both the bacteria. However, the MIC values for a plain solution of a drug combination were observed to be 0.063 mcg/mL for *S. aureus* and 0.125 mcg/mL for *S. epidermidis*. This indicated that the liposome formulation was effective at a lower concentration than the plain solution of the drug combination.<sup>20</sup>

The anti-comedogenic efficacy testing of 1% clindamycin liposomes and 1% plain clindamycin solution revealed that 33.3% of patients on liposome treatment got rid of blackheads (open comedones) safely, whereas with plain clindamycin solution, only 8.33% of patients showed effect. The liposomal clindamycin was also efficacious for closed comedones, pustule, and papules. Another clinical study conducted using the conventional solution, a non-liposomal lotion and liposomal lotion of the same drug showed a 42.9%, 48.3%, and 62.8% decrease in the acne lesion respectively. The study showed higher efficacy of the liposomal formulation.<sup>21,22</sup>

The MIC and Minimum Bactericidal Concentration (MBC) value of azelaic acid ethosomes was found to be 250 mcg/ml for *P. acnes*. However, the MIC and MBC values for the marketed cream (Zelface cream) were found to be 250 mcg/ml and 500 mcg/ml respectively. The azelaic acid ethosomes were proved to be more efficacious than the marketed cream.<sup>23</sup> The actives for the control of acne along with their mechanism, side effects, physicochemical characteristics and stability problems that indicates the necessity of encapsulation are described in Table 1.

### Liposomes in Skin Whitening Therapy

Approximately 15% of the population spends on skin whitening with Asia being the most dominated amongst all. The exposure of skin to the highly energetic UV-B and less energetic UV-A causes melanin synthesis in the melanocytes. The exorbitant synthesis of melanin leads to skin complications such as solar lentigines, melasma, freckle cancer and post-inflammatory intense pigmentation. The enzyme tyrosinase is a key factor that



**Figure 3:** The mechanism of action of liposomes A. In acne treatment B. In hyperpigmentation C. As sunscreen D. As a moisturiser.

synthesises melanin, skin-lightening actives reduce melanin in the skin.<sup>42</sup>

The N-[(2-hydroxy-3-trimethylammonium) propyl] chitosan chloride (HTCC) coated liposomes encapsulated with kojic acid rendered the better fusibility and penetration of liposomes with the membranes of L929 fibroblast cells and B16-F10 melanoma cells due to their positively charged surface than uncoated liposomes. Liposomes coated with HTCC demonstrated a higher melanin synthesis inhibitory activity in B-16-F10 melanoma cell lines over the uncoated liposomes.<sup>43</sup>

Artocarpus Lakoocha (AL) liposomes were evaluated by a double-blind study on female volunteers using a 2% w/w lotion of liposomes containing AL and plain AL extract. After 4 weeks,

the observed lightness values for the liposomes-containing preparation and plain AL extract were found to be 1.37 and 0.89%, respectively, whereas the observed individual topological angle (ITA) values for both the preparations were 6.59 and 5.17%, respectively. The liposomes containing AL preparation were observed to have concentration-dependent skin lightening efficacy. It worked by 77% inhibition of tyrosinase. However, the estimated glutathione inhibition was only 50%.<sup>44</sup>

The flexible liposome containing Niacinamide (NA) known as Bounsphere™ showed the highest skin permeability and enhanced skin whitening than the traditional liposomes. The skin whitening activity of Bounsphere™ was evaluated on human subjects with melasma. The amount of melanin (M-values) in the skin after 4 weeks and 8 weeks was remarkably increased

by 9.96% and 16.80%, respectively, with negligible irritation potential compared with the M-values before NA treatment.<sup>45</sup>

The liposomes loaded anthocyanin showed suppression of tyrosinase, MTF (Microphthalmia-associated transcription factor protein expression) and melanogenesis when studied on Human A 375 melanocytes. The DPPH scavenging activity of liposome-encapsulated anthocyanin was found to be 64% at a concentration of 20 mg/ml and 76% at 50 mg/ml. However, for plain anthocyanin, it was 11% and 24% at concentrations 20 and 50 mg/ml respectively. This reveals the higher antioxidant potential of liposome-encapsulated anthocyanin. The same formulations were studied for cellular tyrosinase activity at concentrations of 5, 10, 20 and 50 mg/ml. The liposome-encapsulated anthocyanin showed concentration-dependent tyrosinase inhibitory activity of 14%, 27%, 48% and 52%, respectively. This inhibition was greater over plain anthocyanin, which was observed to be 5%, 12%, 19%, and 30% at the respective concentrations.<sup>46</sup> Actives used in the treatment of hyperpigmentation along with their mechanism, side effects, physicochemical characteristics and stability problems are described in Table 2.

## Liposomes as Moisturizer

The facial skin possesses a higher level of hydration and is comprised of Natural Moisturizing Factors (NMF). If NMF is absent in the horny layer of skin, water on its own cannot maintain the adequate elasticity of the skin. The moisturizers prevent skin damage, restore skin elasticity and maintain the barrier function.<sup>55,56</sup>

The phospholipids of liposome vesicles intermingle with creatinine in the horny layer and strengthen the skin's barrier, thus minimizing Trans-Epidermal Water Loss (TEWL).<sup>57</sup> The liposome vesicles are capable of elevating skin humidity with the aid of their lipidic additives and thereby preventing premature ageing.<sup>58</sup> In one study, the phosphatidylcholine at concentrations of 0%, 10%, 28%, and 80% on the human subjects showed remarkable differences in the moisture elevation. The formulation with 80% of phosphatidylcholine showed a higher degree of moisture over others. Since these formulations differ in terms of phosphatidylcholine concentration, it is confirmed that the moisturizing effect is due to phosphatidylcholine. The hydrogenated soybean phosphatidylcholine was also found to

**Table 1: Overview of anti-acne actives along with their mechanism of action, characteristics, side effects, and stability issues.**

Actives	Mechanism	Side effects	Physicochemical characteristics	Stability	References
Clindamycin	Bacteriostatic, effective against <i>P. acnes</i> . Lipase production inhibitor, Leukocyte chemotaxis inhibitor.	Skin rashes.	Poor aqueous solubility. Low logP value	Degradation at pH 4 by amine hydrolysis, thioglycoside hydrolysis.	24-26
Tretinoin, isotretinoin	Suppression of hyper cornification, normalization of enzyme metalloproteinases, an inhibitor of (Toll-like receptor) TLR-2.	Skin irritation, burning.	Poor aqueous solubility. Tretinoin permeates the human skin faster than its geometric isomer isotretinoin.	Photodegradation, affected by oxygen, light, acids.	16,25,27
Azelaic acid	Protein synthesis inhibitor in <i>S. epidermidis</i> , change in the intracellular pH of <i>P. acnes</i> , Staph. Epidermidis.	Keratosis pilaris, vitiligo, skin redening.	Poor aqueous solubility. Limited penetration across stratum corneum.	Photooxidation in the presence of nitrate.	28-32
Lauric acid	Strong Antimicrobial activity against <i>P. acnes</i> than BPO. Bacteriostatic, Bactericidal.	Nontoxic.	Low aqueous solubility. Ester form has a high HLB and low logp value.	Hydrolytic rancidity, oxidation, ketonic rancidity, fungus is a major cause of spoilage.	33-37
Adapalene	Microbial collagenase inhibitor, retinoic acid receptor agonist, protein synthesis antagonist.	Erythema, scaling, dryness, burning.	Low percutaneous flux through skin. lipophilicity helps penetration into pilosebaceous follicles in acne.	Degradation on photolytic irradiation, acidic, oxidative degradation.	38-41

**Table 2: Overview of active skin whiteners along with their mechanism of action, characteristics, side effects, and stability issues.**

Actives	Mechanism	Side effects	Physicochemical characteristics	Stability	References
Hydroxyquinone	Competitive inhibitor of melanin production by Covalently linking to histone protein, By Interaction with copper. Acting as a inferior substratum for tyrosinase. Causes permanent harm to melanosomes and melanocytes.	Dermatitis, irritation, erythema, Burning, depigmentation, on long term usage leads to bluish black discolouration of skin.	Less aqueous solubility, less O/W partition value.	Air, light causes oxidation and darkening of colour.	42,47-49
Kojic acid	It is a copper ion chelator and slow acting tyrosinase inhibitor.	Contact allergy	Highly soluble in water, Poor cell penetration.	Sensitive to light and heat instability under aerobic environment.	43,48,50,51
Alpha-tocopherol	Antioxidant.	Safer chemical	Poorly soluble in water, minor permeability through human cadaver skin.	Sensitive to atmospheric oxygen.	52,53
Linoleic acid	Decrease in tyrosinase level.	Mild irritation of skin, eyes.	Low solubility in aqueous solution.	Oxidised by air, sensitive to light.	54
Niacinamide	Preventing melanosome transport to keratinocytethence limits melanin synthesis.	Skin irritant.	Does not easily penetrate through the skin.	Stable to UV, heat, oxygen, acids, bases.	45

stabilize the skin barrier and penetrate as much as the horny layer of skin with lowering TEWL.<sup>59</sup>

A SOPHY liposomal gel (consisting of encapsulated active ingredients such as L-arginine, Curcuma extract, hyaluronic acid, lactic acid, and tocopherol) was found to decrease TEWL and increase skin hydration when examined on healthy human subjects during a 28-day study. The skin moisture level rose by 6.3% in the first seven days of the study. Whereas skin moisture levels were raised by 14.1%, 30.3%, and 33.5% after the second, third, and fourth weeks of gel application, respectively, with minimal erythema index. It also renders higher resistance against bacterial infections by shifting skin pH towards the acidic side.<sup>57</sup>

There are some pieces of evidence that liposomal lotion and non-liposomal lotion have similar potential in reducing xerosis. The effectiveness of plain 12% ammonium lactate lotion and liposomal moisturizing lotion in the management of xerosis was studied by a double-blind clinical trial. Both the formulations were applied twice a day for four weeks. They showed insignificant differences in reducing xerosis. Though both the formulations have shown similar outcomes, liposomes are always preferred when there is a desire to deliver molecules with irritation potential.<sup>60</sup> Some phospholipid-based commercial carrier

systems are stated in Table 3. which inherently has moisturizing properties.

### Liposomes in Sunscreen

Long-term exposure to high energy UV light leads to photoaging, sunburn, actinic keratosis, solar lentigines, melanocytic hyperplasia, immune system suppression, pre-carcinoma and carcinoma lesions on the skin, mostly on the uncovered skin.<sup>63</sup>

The sunscreens are not meant for systemic absorption, but some conventional formulations are reported to be absorbed systemically after topical application. Encapsulation of such candidates into the liposomes provides higher SPF and prevents systemic absorption by retaining them in the horny layer of the skin. The liposome-encapsulated Octyl p-methoxycinnamate (OMC) showed  $22.64 \pm 7.55$  mcg/cm<sup>2</sup> of OMC in the horny layer. It indicates minimal systemic absorption of OMC. However, the value observed for the traditional formulation was  $14.57 \pm 2.30$  mcg/cm<sup>2</sup>.<sup>64</sup>

The protective effect of the liposomal suspension having SPF 50+, 30, 25, 15 was determined using adult skin having Fitzpatrick skin type II at the approved concentration of 2 mg/cm<sup>2</sup>. When the skin was subjected to normal water, salt-water and examined after sweating, it was observed that the SPF 50+ of the liposomal

**Table 3: Commercial liposomal carriers with moisturizing properties.**

Lipoidal carrier	Composition	Characteristics	References
Lysofix™	Glycerine, Glycine Soja (Soyabean) Seed extract.	Improves pigment dispersion, minimizes TEWL, enhances skin penetration and bioavailability of actives, highly tolerable.	61
Lecigel™	Sodium Acrylates Copolymer, Lecithin.	Emulsifying properties, minimizes TEWL, improves skin moisture level.	61
Amisol™ Soft	Behenyl Alcohol, Glyceryl Stearate, Lecithin, Glycine Soja (Soybean) Sterols.	O/W lamelliform emulsifier, highly tolerable and improves skin moisture level, Boosts effectiveness and bioavailability of actives.	61
Biophilic™ S MB	Lecithin, C-12 to C-16 alcohols, hexadecanoic acid.	O/W lamelliform emulsifier, minimizes TEWL, highly tolerable, increases bioavailability of actives.	61
Heliofeel™	Glyceryl Stearate Citrate, Polyglyceryl-3 Stearate, Hydrogenated Lecithin.	Moisturizes the skin, Decreases TEWL, increases penetrability and bioavailability of actives.	61
Natipide® II	Phospholipid from soyabean, ethanol, water.	Improves skin humidity and skin penetration.	59,62

**Table 4: Overview of sunscreen molecules along with their mechanism of action, characteristics, side effects, and stability issues.**

Actives	Mechanism	Side effects	Physicochemical characteristics	Stability	References
Benzophenone	Absorption of UVA, UVB.	Slightly irritating.	Water insoluble, combustible.	Emits acrid and irritating fumes on heating.	67,68
Para amino benzoic acid	Absorbs UV light and emits less energy.	Rarely Eczema, redness, stinging, burning.	Low partition coefficient.	Discolouration on exposure to light.	67,69
Avobenzone	Blocks UVA-I, UVA-II, UV-B.	Rarely Eczema, redness, stinging, burning.	Insoluble in water.	Sensitive to light.	70
Zinc oxide	A physical blocker. Reflects, scatter and absorbs UV light.	Rarely Eczema, redness, stinging, burning.	Insoluble in water.	On heating emits toxic fumes of zinc oxide, slowly decomposed by water.	71-73
Titanium dioxide	A physical blocker of UV-A and UV-B, have high refractive indices.	Nontoxic, non-irritant.	Insoluble in water and organic solvents. it is shown to induce photooxidation of unsaturated lipids.	Extremely stable at high temperature.	71,73-75

sunscreens had declined very slightly to 97% in normal water, 96% in salt-water and 99% after sweating. However, the SPF 30 of another liposomal sunscreen was reduced to 97% in normal water, 96% in salt-water and 99% after sweating. While the liposomal sunscreen formulation has SPF 25, the SPF value declined to 90% in normal water, 83% in salt-water and 91% after sweating. The observed SPF of the liposomal sunscreen formulation with SPF 15 was declined to 96% in normal water, 96% in salt-water and 95% after sweating. The study concluded that SPF 50+ showed more major resistance than SPF 15, but the resistance shown by liposomal sunscreen with SPF 15 was more

than the in-house control having SPF 15 against normal water, salt-water, and sweating.<sup>65</sup>

The inactive ingredients used in the liposomes also have noticeable role for sunscreen action. Multilamellar liposomes of Ethyl hexyl methoxycinnamate (EHMC) was prepared by using hydrogenated phosphatidylcholine (HPC) and internal wool lipids (IWL) did not show any penetration in the skin barrier over phosphatidylcholine liposomes and o/w emulsion of the same drug. The study confirmed a better potential of HPC and IWL liposomes to stay at the horny layer of the skin with

**Table 5: Marketed liposomal skin care formulations along with their composition and role.**

Products	Composition	Role				References
		Anti-acne	Skin lightening	Moisturizing, nourishing	Sunscreen	
Citrolumine 8 <sup>®</sup> cream by Lipoid kosmetik.	Extract from citrus fruit.		Yes	Yes		77
Cetaphil sunkids <sup>®</sup> liposomal lotion SPF 50+.	Pantothenol, glycerine, aloe vera, Vitamin E.			Yes	Yes	78
Liposome Proteos <sup>®</sup> oil free formula by Martiderm.	Proteoglycans, vitamin C, Vitamin E, Hamamelis virginiana L.	Yes		Yes		79
Lipocoll <sup>®</sup> serum pro by Larens.	Natural fish collagen peptide and amino acids.			Yes		80
Azelac Ru <sup>®</sup> liposome cream and serum by Sesderma.	azelaic acid.	Yes	Yes			81
Lancome <sup>®</sup> noisome cream by L'Oréal.	Linseed extract, Lipo hydroxy acid (LHA).		Yes	Yes		82

minimal percutaneous absorption by the HPC.<sup>66</sup> The sunscreen actives along with their mechanism, side effects, physicochemical characteristics and stability problems are described in Table 4.

## MARKET FOR SKIN CARE LIPOSOMES

The liposome cosmetic market size and share report 2021 stated that the worldwide liposome cosmetics marketplace was worth 2861.58 million USD in 2020 and could grow with a CAGR of 7.67% from 2020 to 2027. Lipoid cosmetic firm, Lucas Meyer Cosmetic firm, Nippon Fine Chemical company, Enoc Pharma enterprise, Nanovec manufacturers, and Lipotec Company are a few of the major players in the liposomal cosmetic market.<sup>76</sup> The commercial liposomal skin care cosmetics that are available in the market are quoted in Table 5.

## REGULATIONS FOR NANOCOSMETICS

The US FDA's (Federal Food and Drug Administration) Centre for Drug Evaluation and Research (CDER) functions by reviewing the New Drug Application (NDA) and Abbreviated New Drug Application (ANDA) applications for liposome drug products.

According to US FDA, it is not mandatory to register the cosmetic enterprise and products by the manufacturer. The FDA issued the protocol regarding manufacturing, physicochemical testing,

end-product testing, pharmacokinetic testing and post-approval changes for liposomal products. To ensure the safety and quality of nano-cosmetics, the manufacturer should adhere to the regulations set by the country. The US FDA does not claim any product as "cosmeceuticals". It stated that products like moisturisers containing sunscreen agents should be considered drugs. The products used in acne therapy and sunscreens are declared as non-prescription drugs. However, the European regulatory authorities have categorised sunscreens as cosmetics. In India, CDSCO, the central licencing authority, recognises drugs and cosmetics as a separate class.<sup>84,85</sup>

## CONCLUSION

The extensive atmospheric and lifestyle changes demand the need for skin care on a priority basis. Conventional skincare formulations lack satisfactory performance due to formulation constraints. The liposome vesicles have shown outstanding performance in drug delivery to the skin. They are widely used in skin protective products like moisturizers, sunscreen, and curative products such as anti-acne and skin lightening therapy. They are been found to be biocompatible, biodegradable and safe as compared to conventional therapy. As cosmeceutical industry is growing, there is increasing need for stringent regulations to



be set and followed by the respective countries to make safe and effective nano-cosmetics.

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## CONFLICT OF INTEREST

The authors declare no conflict of interests.

## ABBREVIATIONS

**P. acnes:** *Propionibacterium acnes*; **DPPC:** Dipalmitoylphosphatidylcholine; **ATCC:** American Type Culture Collection; **MIC:** Minimum Inhibitory Concentration; **S. epidermidis:** *Staphylococcus epidermidis*; **MBC :** Minimum Bactericidal Concentration; **mcg/mL:** Microgram per Milliliter; **TLR-2:** Toll-like Receptor; **BPO:** Benzoyl peroxide; **HLB:** Hydrophilic Lipophilic Balance; **UV:** Ultra-violet; **HTCC:** N-[(2-hydroxy-3-trimethylammonium) propyl] chitosan chloride; **AL:** Artocarpus Lakoocha; **ITA:** Individual Topological Angle; **NA:** Niacinamide; **MTFF:** Microphthalmia-Associated Transcription Factor Protein Expression; **DPPH 1:** 1-diphenyl-2-picrylhydrazyl; **mg/mL:** Milligram per Milliliter; **NMF:** Natural Moisturizing Factor; **TEWL:** Trans Epidermal Water Loss; **O/W:** Oil in Water; **OMC:** Octyl p-methoxycinnamate; **SPF:** Sun Protection Factor; **EHMC:** Ethyl Hexyl Methoxycinnamate; **HPC:** Hydrogenated Phosphatidylcholine; **IWL:** Internal Wool Lipids; **USD:** United States Dollar; **CAGR:** Compound Annual Growth Rate; **US FDA:** United States Food and Drug Administration; **CDER:** Centre for Drug Evaluation and Research; **NDA:** New Drug Application; **ANDA:** Abbreviated New Drug Application; **CDSO:** Central Drugs Standard Control Organization.

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